

## **Dominant Preaxial Brachydactyly with Hallux Varus and Thumb Abduction**

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### **INTRODUCTION**

Brachydactyly, or shortening of the digits due to an anomalous development of phalanges or metacarpals, has received much attention from students of human genetics because it is readily visible, often present in multiple family members, and occurs in a wide variety of genetically true phenotypes. Haws and McKusick [1] credit Farabee [2] with interpreting shortening of the middle phalanges as the first Mendelian dominant trait in man. Bell [3] classified seven types of brachydactyly based upon anatomic and genetic grounds. Parish [4] and Poznanski et al. [5] have recorded measurements from radiographs of normal hands allowing a systematic definition of what is normal and a multivariate delineation of abnormalities.

Future studies of brachydactyly should provide a better understanding of the genes involved in embryogenesis of the extremities. This communication describes a dominant form of preaxial brachydactyly that is associated with hallux varus and abducted thumbs.

### **FAMILY STUDY**

Family no. 750 (fig. 1) came to our attention because of an infant (V-14) who, like several other family members, had brachydactyly, hallux varus, and abducted thumbs. The major complaint of affected family members was that the hallux varus made it difficult to wear shoes.

The proband (V-14) was the product of a normal term pregnancy and at birth

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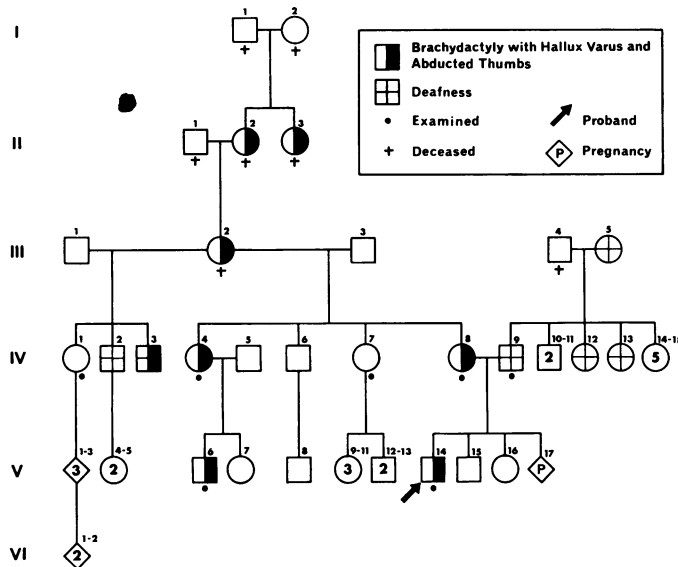


FIG. 1.—Pedigree of family no. 750

was noted to have abnormal hands and feet. Physical examination at 6 years of age revealed a 23-kg male who was 118 cm tall and had obvious hand and foot anomalies but no other striking physical findings. Stanford-Binet intelligence testing gave IQs ranging from 68 to 83. He had a normal audiogram, blood count, and chest roentgenogram. Urinalysis was normal, including screening for reducing substances, sulfhydryl groups, keto-acids, glycosaminoglycans, and amino acids.

The proband's mother (IV-8), born in 1937, has extremity malformations virtually identical with those of her son. Her height is 140 cm. She has gone through three uneventful pregnancies and is now pregnant for the fourth time. She is apparently mentally retarded, has had only 1 year of formal schooling, but apparently functions adequately as a mother and wife. Cephalometric roentgenograms were within normal limits, as were urine screening for reducing substances, sulfhydryl groups, keto-acids, and glycosaminoglycans. Urinary amino acid electrophoresis revealed a generalized aminoaciduria which was attributed to her pregnancy.

Individual IV-4, born in 1938, is 145 cm tall. She did very poorly in school, completing only the seventh grade. She has a history of repeated urinary tract infections since age 15. At age 23 she underwent a left nephrolithotomy, and at age 31 had bilateral nephrolithotomies at which time stones were removed containing 90% urinary apatite [ $\text{Ca}_{10}(\text{PO}_4, \text{CO}_3\text{OH})_6(\text{OH})_2$ ] and 10% whitlockite [ $\text{Ca}_3(\text{PO}_4)_2$ ]. At age 31 she had moderately impaired renal function (creatinine clearance 43 ml/min, normal = 90–130). Surgery, intravenous pyelography, and retrograde pyelography were all consistent with chronic pyelonephritis and nephrolithiasis, but there were no obvious congenital anomalies of the kidneys or urinary tract.

Laboratory findings included normal serum calcium, phosphorus, chloride, potassium, sodium, uric acid, albumin, and globulins. Roentgenograms of the chest, arms, and legs were normal. She had a normal audiogram and electrocardiogram.

Individual V-6, born in 1959, weighed 25 kg at age 11 and was 128 cm tall. He has difficulty with school work, and at age 10 a Stanford-Binet psychological evaluation revealed an IQ of 60. Roentgenograms of the skull, long bones, and chest were within normal limits.

Figure 2A is a plantar view of the proband's (V-14) feet taken in infancy showing the extreme hallux varus. A dorsal view of his cousin's feet (V-6) taken at age 7 is shown in figure 2B; and figure 2C is a similar view of the proband's mother's (IV-8) feet, illustrating the foot anomalies at varying ages. Of the four affected members examined, only V-6 had 2-3 syndactyly of the toes.

Figures 2D and 2E show the hands of individuals IV-4 and V-14, respectively, with the short abducted thumbs and relatively broad thumbnails. There also appears to be shortening of the index fingers and perhaps the third finger, but the fourth and fifth fingers appear normally proportioned. There also is widening of the 2-3 interdigital spaces.

Roentgenograms of the feet of individual IV-4 are shown in figure 2J. A mild forefoot varus is present as it was in the other affected family members but the tarsal bones appear normal. The first metatarsal is broad and short, and in the adults examined (IV-4 and IV-8) abutted distally against the second metatarsal producing a pseudoarticulation. This was perhaps secondary to forced adduction of the great toes by shoes. Metatarsals 2-5 appear normal. The varus deformity of the great toe is associated with articulation of the proximal phalanx with the medial (preaxial) aspect of the malformed and shortened first metatarsal. In all family members examined the middle and distal phalanges of the toes appeared broader than normal when compared with their length.

Figure 2G is a hand roentgenogram of individual IV-4. The following findings were noted in the roentgenograms of individuals IV-4 and IV-8. The carpals were normal except for minor irregularity of the articular surface of the greater multangular. The first metacarpals were unusually broad and short, the phalanges of the thumb deviated radially (preaxially) associated with a radially placed articulation with the metacarpal, and metacarpals 2-5 had increased cortical thickness. The middle and distal phalanges of the fingers were relatively wide but had increasingly normal proportions toward the ulnar (postaxial) side of the hand.

Figure 2H is a roentgenogram of the hands of individual V-6 taken at 10 years of age. Like individual V-14, he had a normal bone age. In contrast to their mothers, V-6 and V-14 had no evidence of thickened metacarpal cortices. Neither boy had secondary ossification centers of the first metacarpals.

All four individuals examined had a deep distal transverse palmar crease that extended to the distal border of the palm and terminated between the second and third digits (fig. 2F). A similar distal transverse crease occurs in 18% of normal individuals [6], but in this family its depth and association with a widened space between digits 2 and 3 remove it from the range of normal variation.

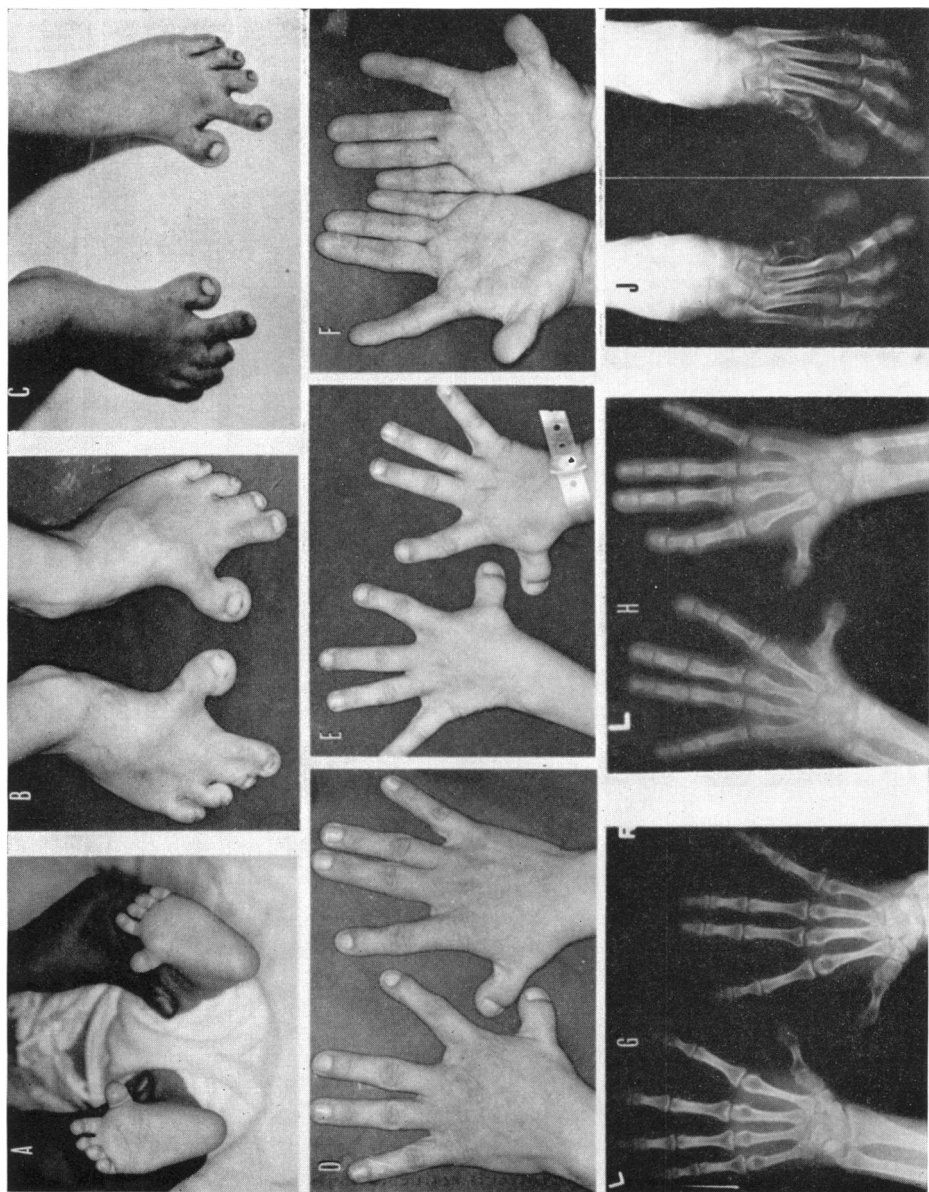


FIG. 2.—A, Feet of individual V-14, 3 months of age. B, Feet of individual V-6, age 7. C, Feet of individual IV-8, age 29. D, Hands of individual IV-4, age 31. E, Hands of individual V-14, age 6. F, Hands of individual IV-4, palmar view, age 31. G, Hand roentgenogram of individual IV-4, age 31. H, Hand roentgenogram of individual V-6, age 10. J, Foot roentgenogram of individual IV-4, age 31.

Inability to wear shoes led to surgical correction of the hallux varus in individuals V-6 and V-14. The operative technique of McElvenny [7] was used in which fibrous tissue on the medial side of the toes was excised, followed by a lateral exostosectomy of the proximal phalanx of the great toe and osteotomy of the first metatarsal shaft, allowing straightening of the toe which was then fixed in position by an internal wire. The first and second toe were then partially syndactylized and a short leg cast applied. The correction was successful in both boys. Figure 3 shows the right foot of individual V-6 pre- and postoperatively.

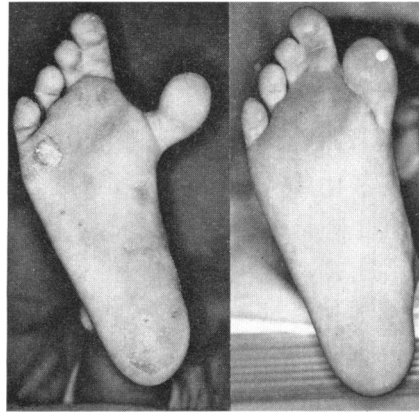


FIG. 3.—Right foot of individual V-6, before and after treatment

#### DISCUSSION

The present family's relatively broad angulated thumbs superficially resemble those of patients with the broad-thumbs syndrome or the Rubinstein-Taybi syndrome [8]. However, closer inspection reveals that patients with the Rubinstein-Taybi syndrome have angulation of the thumbs at the interphalangeal joint with relatively normal first metacarpals while the present family has angulation at the metacarpal-phalangeal joint and extremely short first metacarpals. Patients with diastrophic dwarfism have first metacarpal shortening, similar to the present family [9], but, in addition, have generalized and severe shortening of the extremities.

The striking feet changes found in this family are somewhat like those of the oto-palato-digital (OPD) syndrome with bulbous toes and relatively long second toes [10]. The OPD syndrome is not, however, characterized by the hallux varus and shortening of the first metacarpals found in the present family. The foot findings in this and in the OPD syndrome are, however, similar enough to be included in the differential diagnosis of "treefrog toes."

Hallux varus is a rare, generally unilateral birth defect, and a review of reported cases reveals great variability of anatomic malformations reported with hallux varus. Farmer [11] reported several cases associated with duplication of the phalanges or metatarsals of the great toe. Horwitz [12] reported a case of bilateral

ectrodactyly as hallux varus. Haas [13] reported unilateral hallux varus with ipsilateral shortening of the first metatarsal, and Sloan [14] reported a case of unilateral hallux varus with otherwise normal bony structure. Satzepin [15] reported a boy with bilateral hallux varus and short first metacarpals whose roentgenogram findings were much like those in the present family with the exception that the distal phalanges were not shortened. Also, no mention was made of similar hand malformations and there was no family history of other affected individuals.

Our family does not fit into Bell's [3] classification of brachydactyly but seems to encompass Bell's types D and E. Bell's type D is characterized by shortening of the terminal phalanges of the thumbs and big toes and type E by shortening of the metacarpals with or without shortening of the metatarsals.

Poznanski et al. [5] calculated the relative proportions of the bones of the thumb in both sexes and by age groups. Table 1 compares these normal ratios with find-

TABLE 1

RELATIVE LENGTHS OF BONES OF THE THUMB IN MEMBERS OF FAMILY No. 750  
COMPARED WITH THE FIRST AND SECOND METACARPALS

	IV-4	IV-8	Normal Adult Female*	V-6	Normal Male* (9 yr)	V-14	Normal Male* (4 yr)
Met 1/Met 2 .....	0.38	0.41	0.58-0.74	0.42	0.62-0.70	0.44	0.60-0.68
Met 1/P1 .....	0.73	0.74	1.31-1.51	0.84	1.37-1.61	0.76	1.29-1.53
Met 1/D1 .....	1.64	1.77	1.75-2.23	1.77	1.72-2.12	1.31	1.62-2.02
P1/Met 2 .....	0.52	0.55	0.41-0.53	0.50	0.40-0.48	0.58	0.41-0.49
D1/Met 2 .....	0.23	0.23	0.29-0.37	0.24	0.30-0.38	0.33	0.31-0.39
D1/P1 .....	0.44	0.42	0.63-0.79	0.48	0.70-0.86	0.57	0.69-0.85

NOTE.—Met 1 = metacarpal of the thumb; P1 = proximal phalanx of the thumb; D1 = distal phalanx of the thumb.

\* Mean  $\pm$  2 sd [5].

ings in the present family. These comparisons show striking shortening of the distal phalanx of the thumb and first metacarpal when compared with the proximal phalanx of the thumb and the second metacarpal. These comparisons, however, are only relative and do not give absolute comparisons of bone lengths.

The data of Parish [4] were used to compare the affected adult females in family no. 750 with normal absolute values (fig. 4). These comparisons show that the proximal phalangeal lengths are within normal limits while the first metacarpal and distal phalanges are extremely short. There is also some shortening of the second and third metacarpals and distal phalanges, but the fourth and fifth are within normal limits. Comparison of the middle phalangeal lengths for individuals IV-4 and IV-8 with data of Garn et al. [16] reveals that they are all within normal limits.

In the present family, brachydactyly appears to be segregating as a Mendelian dominant trait that results in shortening of the distal phalanges, metacarpals, and

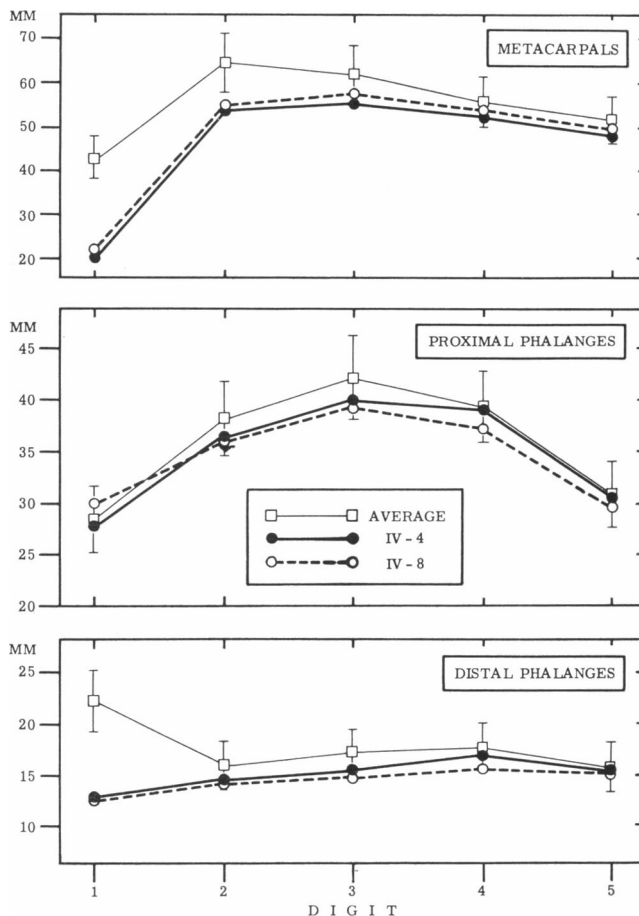


FIG. 4.—Comparison of phalangeal and metacarpal lengths of individuals IV-4 and IV-8 with normal averages  $\pm 2$  SD [4, 16].

metatarsals on the preaxial side of the extremities, but skips the proximal and middle phalanges. While the thumbs and great toe are most affected by the abduction and brachydactyly, there is some increased abduction of the second digits and shortening of the second and third digits of both hands and feet, indicating a gradient of effects pre- to postaxially.

In family no. 750, no males have reproduced so there is no chance for male-to-male transmission which would rule out X-linkage. However, affected males do not appear to be more severely affected than females which is suggestive of an autosomal rather than an X-linked trait. All four of the affected individuals examined appear to have mild mental retardation and by history are mentally slower than their siblings. For example, individual IV-6 has a college education. Impaired intellectual development may therefore be a part of this syndrome. By history there are six deaf individuals in this family (fig. 1). However, only one of eight

individuals reported with brachydactyly is deaf, so deafness was considered to be genetically unrelated to the brachydactyly.

#### SUMMARY

A family is reported in which eight members of four generations have brachydactyly of the thumbs and great toes associated with abduction of these same digits. There is less severe brachydactyly of the second and third digits of the hands and feet and some abduction of the second digits. The brachydactyly is due to shortening of the metacarpals, metatarsals, and distal phalanges while the proximal and middle phalanges are of normal length.

Inheritance is compatible with a dominant trait with males and females similarly affected. The affected family members appear to be mentally retarded with IQs in the 60-80 range.

ADDED IN PRESS.—Since the manuscript was submitted, the pregnancy shown in figure 1 (individual V-17) has resulted in an apparently normal male infant.

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